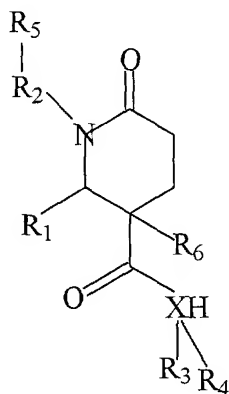


WE CLAIM:

1. A combinatorial library of two or more compounds of the formula:



wherein:

X is selected from the group consisting of N and H;

R₁ is selected from the group consisting of a substituted aromatic heterocyclic ring, C₃-C₁₂ substituted alicycle and substituted phenyl;

R₂ is selected from the group consisting of C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₂-C₇ alkenyl; C₁ to C₇ substituted alkenyl; C₂ to C₇ alkynyl; C₂ to C₇ substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C₂ to C₇ heterocyclic ring; substituted C₂ to C₇ heterocyclic ring; substituted cyclic C₂ to C₇ alkylene; C₁ to C₆ alkyl; C₁ to C₆ substituted alkyl; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₇ alkoxy; halo; C₁ to C₁₀ alkylthio; C₁ to C₁₀ substituted alkylthio; C₁ to C₁₀ alkyl nitrile; a C₇ to C₁₈ substituted phenylalkyl; and substituted phenyl;

R₃ and R₄ are independently selected from the group consisting of -OH; H; C₁ to C₆ alkyl; C₁ to C₆ substituted alkyl; C₂ to C₇ alkenyl; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₁₀ alkylthio; C₁ to C₁₀ alkyl nitrile; C₁ to C₄ alcohol; phenyl; substituted phenyl; C₁ to C₆ substituted alkyl; C₁ to C₇ alkoxy; C₃ to C₇ cycloalkyl; and C₃ to C₇

substituted cycloalkyl; C₂ to C₇ heterocyclic ring; C₂ to C₇ substituted heterocyclic ring; phenoxy; and substituted phenoxy,

R₅ is selected from the group consisting of H and NH₂, and

R₆ is selected from the group consisting of phenyl, substituted phenyl, C₂ to C₇ heterocyclic ring, and substituted C₂ to C₇ heterocyclic ring;

and wherein

said C₁ to C₆ substituted alkyl, said C₁ to C₄ substituted alkylthio and said C₁ to C₇ substituted alkoxy are substituted by one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, oxo, protected oxo, C₃ to C₇ cycloalkyl, naphthyl, amino, protected amino, substituted amino, protected substituted amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C₁ to C₇ alkoxy, C₁ to C₇ acyl, C₁ to C₇ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N,N-di(C₁ to C₆ alkyl)carboxamide, cyano, methylsulfonylamino, thiol, phenyl, substituted phenyl, C₁ to C₄ alkylthio and C₁ to C₄ alkylsulfonyl groups,

said C₃ to C₇ substituted cycloalkyl is substituted by one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, C₁ to C₄ alkylthio, C₁ to C₄ alkylsulfoxide, C₁ to C₄ alkylsulfonyl, C₁ to C₄ substituted alkylthio, C₁ to C₄ substituted alkylsulfoxide, C₁ to C₄ substituted alkylsulfonyl, C₁ to C₆ alkyl, C₁ to C₇ alkoxy, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, oxo, protected oxo, substituted amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, and protected amino groups,

said substituted phenyl, substituted aromatic heterocyclic ring and substituted alicycle are substituted with at least one substituent independently selected from the group consisting of H, halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, C₁ to C₇ substituted alkoxy, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, thio, C₁ to C₇ alkylthio,

C₁ to C₇ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N, N-di(C₁ to C₆ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₆ alkyl)sulfonyl)amino, NB(phenylsulfonyl)amino, phenyl and substituted phenyl, said substituted amino is substituted with one or two substituents independently selected from the group consisting of phenyl, substituted phenyl, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, C₂ to C₇ alkenyl, C₂ to C₇ substituted alkenyl, C₂ to C₇ alkynyl, C₂ to C₇ substituted alkynyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl and a heterocyclic ring,

said substituted phenoxy is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino and N-(phenylsulfonyl)amino,

said C₇ to C₁₈ substituted phenylalkyl and said C₁ to C₁₂ substituted heterocycloalkyl are substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, substituted amino, protected substituted amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-(C₁ to C₁₂ dialkyl)carboxamide, cyano, N-(C₁ to C₁₂

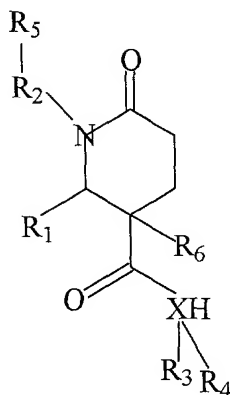
alkylsulfonyl)amino, thiol, C₁ to C₁₀ alkylthio, and C₁ to C₁₀ alkylsulfonyl; and if substituted any phenyl group is substituted with at least one substituent independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, cyclic C₂ to C₁₂ alkylene and a substituted or unsubstituted phenyl group, and

said substituted heterocyclic ring is substituted with at least one substituent independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, heterocycle and substituted heterocycle.

2. The combinatorial library according to claim 1, wherein said C₁ to C₆ substituted alkyl is substituted with at least one substituent selected from the group consisting of thiol, halo, C₁ to C₆ alkoxy, and phenyl unsubstituted or substituted with a substituent selected from the group consisting of halo and C₁ to C₆ alkoxy.

3. The combinatorial library according to claim 1, wherein R₁ is a substituted phenyl.

4. The combinatorial library according to claim 1, wherein R_5 is H.
5. The combinatorial library according to claim 1, wherein R_5 is NH_2 .
6. A compound of the formula:



wherein:

X is selected from the group consisting of N and H;

R_1 is selected from the group consisting of a substituted aromatic heterocyclic ring, C_3 - C_{12} substituted alicycle and substituted phenyl;

R_2 is selected from the group consisting of C_1 to C_7 alkoxy; C_1 to C_7 substituted alkoxy; C_2 - C_7 alkenyl; C_1 to C_7 substituted alkenyl; C_2 to C_7 alkynyl; C_2 to C_7 substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C_2 to C_7 heterocyclic ring; substituted C_2 to C_7 heterocyclic ring; substituted cyclic C_2 to C_7 alkylene; C_1 to C_6 alkyl; C_1 to C_6 substituted alkyl; C_3 to C_7 cycloalkyl; C_3 to C_7 substituted cycloalkyl; C_1 to C_7 alkoxy; halo; C_1 to C_{10} alkylthio; C_1 to C_{10} substituted alkylthio; C_1 to C_{10} alkyl nitrile; a C_7 to C_{18} substituted phenylalkyl; and substituted phenyl;

R₃ and R₄ are independently selected from the group consisting of –OH; H; C₁ to C₆ alkyl; C₁ to C₆ substituted alkyl; C₂ to C₇ alkenyl; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₁₀ alkylthio; C₁ to C₁₀ alkyl nitrile; C₁ to C₄ alcohol; phenyl; substituted phenyl; C₁ to C₆ substituted alkyl; C₁ to C₇ alkoxy; C₃ to C₇ cycloalkyl; and C₃ to C₇ substituted cycloalkyl; C₂ to C₇ heterocyclic ring; C₂ to C₇ substituted heterocyclic ring; phenoxy; and substituted phenoxy,

R₅ is selected from the group consisting of H and NH₂, and

R₆ is selected from the group consisting of phenyl, substituted phenyl, C₂ to C₇ heterocyclic ring, and substituted C₂ to C₇ heterocyclic ring, and wherein

said C₁ to C₆ substituted alkyl, said C₁ to C₄ substituted alkylthio and said C₁ to C₇ substituted alkoxy are substituted by one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, oxo, protected oxo, C₃ to C₇ cycloalkyl, naphthyl, amino, protected amino, substituted amino, protected substituted amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C₁ to C₇ alkoxy, C₁ to C₇ acyl, C₁ to C₇ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N,N-di(C₁ to C₆ alkyl)carboxamide, cyano, methylsulfonylamino, thiol, phenyl, substituted phenyl, C₁ to C₄ alkylthio and C₁ to C₄ alkylsulfonyl groups,

said C₃ to C₇ substituted cycloalkyl is substituted by one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, C₁ to C₄ alkylthio, C₁ to C₄ alkylsulfoxide, C₁ to C₄ alkylsulfonyl, C₁ to C₄ substituted alkylthio, C₁ to C₄ substituted alkylsulfoxide, C₁ to C₄ substituted alkylsulfonyl, C₁ to C₆ alkyl, C₁ to C₇ alkoxy, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, oxo, protected oxo, substituted amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, and protected amino groups,

said substituted phenyl, substituted aromatic heterocyclic ring and substituted alicycle are substituted with at least one substituent independently selected from the group consisting of H, halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, C₁ to C₇ substituted alkoxy, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, thio, C₁ to C₇ alkylthio, C₁ to C₇ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N, N-di(C₁ to C₆ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₆ alkyl)sulfonyl)amino, NB(phenylsulfonyl)amino, phenyl and substituted phenyl,

said substituted amino is substituted with one or two substituents independently selected from the group consisting of phenyl, substituted phenyl, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, C₂ to C₇ alkenyl, C₂ to C₇ substituted alkenyl, C₂ to C₇ alkynyl, C₂ to C₇ substituted alkynyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl and a heterocyclic ring,

said substituted phenoxy is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino and N-(phenylsulfonyl)amino,

said C₇ to C₁₈ substituted phenylalkyl and said C₁ to C₁₂ substituted heterocycloalkyl are substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, substituted amino, protected substituted amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic

ring, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-(C₁ to C₁₂ dialkyl)carboxamide, cyano, N-(C₁ to C₁₂ alkylsulfonyl)amino, thiol, C₁ to C₁₀ alkylthio, and C₁ to C₁₀ alkylsulfonyl; and if substituted any phenyl group is substituted with at least one substituent independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, cyclic C₂ to C₁₂ alkylene and a substituted or unsubstituted phenyl group, and

said substituted heterocyclic ring is substituted with at least one substituent independently selected from the group consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, heterocycle and substituted heterocycle.

7. The compound according to claim 6, wherein said C₁ to C₆ substituted alkyl is substituted with at least one substituent selected from the group

consisting of thiol, halo, C₁ to C₆ alkoxy, and phenyl unsubstituted or substituted with a substituent selected from the group consisting of halo and C₁ to C₆ alkoxy.

8. The compound according to claim 6, wherein R₁ is a substituted phenyl.

9. The compound according to claim 6, wherein R₅ is H.

10. The compound according to claim 6, wherein R₅ is NH₂.

11. A method of making the compound of claim 6, comprising
preparing a resin bound aldehyde or diamine,
reacting said resin bound aldehyde with an amine, or said resin bound
diamine with an aldehyde, to form a resin bound imine,
cyclizing said resin bound imine to produce a resin bound carboxylic acid,
acylating said resin bound carboxylic acid, and
cleaving and extracting said piperidine-3-carboxamide derivative compound
from said resin.

12. The method according to claim 11, wherein said aldehyde is selected
from the group consisting of 4-hydroxybenzaldehyde, 3-hydroxybenzaldehyde, 2-
hydroxy-5-methylbenzaldehyde, 3,5-dimethyl-4-hydroxybenzaldehyde, 2-
hydroxy-4-methoxybenzaldehyde, 3-ethoxysalicylaldehyde, 2-hydroxy-1-
naphthaldehyde, 5-bromosalicylaldehyde, cyclopropanecarboxaldehyde, 3-
furaldehyde, benzaldehyde, 2-thiophenecarboxaldehyde, 3-
thiophenecarboxaldehyde, P-tolualdehyde, 4,5-dimethyl-2-furancarboxaldehyde,
P-anisaldehyde, 5-methylfurfural, O-tolualdehyde, 2,4,5-trimethylbenzaldehyde,
piperonal, 5-methyl-2-thiophenecarboxaldehyde, 4-
(difluoromethoxy)benzaldehyde, 5-bromo-2-furaldehyde, 4-
biphenylcarboxaldehyde and 5-bromo-2-thiophenecarboxaldehyde.

13. The method according to claim 12, wherein said resin is *p*-benzyloxybenzyl alcohol-polystyrene.

14. The method according to claim 12, wherein said diamine is selected from the group consisting of ethylenediamine, 1,3-diaminopropane, 1,4-diaminobutane, trans-1,2-cyclohexanediamine, and trans-1,4-diaminocyclohexane.

15. The method according to claim 12, wherein said resin bound aldehyde is reacted with an amine selected from the group consisting of methylamine, ethylamine, propargylamine, cyclopropylamine, allylamine, propylamine, 3-aminopropionitrile, isobutylamine, cyclopentylamine, cyclohexylamine, hexylamine, N-acetythylenediamine, 3-ethoxypropylamine, 4-chlorobenzylamine, 1-(3-aminopropyl)-2-pyrrolidinone, tryptamine, 3-(trifluoromethyl) benzylamine, 2,4-dichlorophenethylamine, 4-amino-1-benzylpiperidine, benzylamine, 2,2-thiobis(ethylamine), and N,N-Bis(3-aminopropyl)methylamine.

16. The method according to claim 12, wherein said resin bound carboxylic acid is acylated in the presence of an amine selected from the group consisting of nipecotamide, 1-(2-aminoethyl)pyrrolidine, pyrrolidine, histamine, cyclopentylamine, allylamine, 2-methoxyethylamine, cyclohexylamine, 1-methylpiperazine, tetrahydrofurfurylamine, 4-methylbenzylamine, 3-fluorobenzylamine, 4-fluorobenzylamine, 1-(3-aminopropyl)imidazole, cyclopropylamine, propylamine, ethanolamine, 2-thiophenemethylamine, *n,n*-dimethyl-1,3-propanediamine, 1-(2-aminoethyl)piperidine, isoamylamine, 3-ethoxypropylamine, (*r*)-(-)-1-cyclohexylethylamine, neopentylamine, 3-(methylthio)propylamine, isobutylamine, 3-amino-1-propanol, 2-ethoxyethylamine, 2,6-dimethylpiperazine, propargylamine, thiophene-2-ethylamine, butylamine, 2-amino-1-methoxypropane, 3-aminopropionitrile, 3-methylpiperidine, *P*-anisidine, 1,2,3,6-tetrahydropyridine, 2,6-

dimethylmorpholine, methoxyamine hydrochloride, n-ethylpiperazine, water, and hydroxylamine.

17. The compound according to claim 6, wherein said compound is bound to a polystyrene resin.

18. The compound according to claim 17 wherein said polystyrene resin is PEG-grafted polystyrene resin.

19. The compound according to claim 17, wherein said polystyrene resin is *p*-benzyloxybenzyl alcohol-polystyrene.